SOMATOSTATIN: ALTERATIONS IN NEURODEGENERATIVE DISEASES AND POTENTIAL USEFULNESS IN THE CLINICS, J. Epelbaum, INSERM U.159, Centre Paul Broca, 2ter rue d'Alesia, 75014, Paris, FRANCE.

Since the early eighties, a number of studies convincingly demonstrated that somatostatin concentrations are reduced in the cortex and hippocampus of Alzheimer's disease (AD) patients. However, few studies investigated the causes of this relatively selective neuropeptidergic deficit in relation with the cholinergic impairment and neuropathology of the disease. We quantified these parameters in the brains of 12 women over 75 years of age which ranged from 27 to 1 in the Blessed test score (BTS). The results indicated that the somatostatinergic deficit was more regionally restricted to the frontal pole than the cholinergic ones, also evident in the parietal and temporal lobes. Both somatostatin and CholineAcetylTransferase (ChAT) impairments were related to the intellectual loss but somatostatin was never correlated to the neuropathology (neurofibrillary tangles and senile plaques); in contrast to ChAT which did correlate in the parietal and temporal lobes. Since somatostatin and ChAT were also correlated in the frontal and parietal lobes, these results suggested that cortical somatostatin-containing elements are only affected following the cholinergic ones. By semi-quantitative in situ hybridization, an overall reduction of labeled cell density was observed in patients with AD but a significantly lower level of expression of somatostatin mRNA/cell was only observed in the hippocampus. Thus, the ability of cortical cells to express somatostatin mRNA is partially preserved in AD. Furthermore, the degradation rate of somatostatin by peptidases is lowered in frontal and parietal cortices from AD patients, indicating a compensatory mechanism and ruling out the use of blockers of somatostatin degradation to pharmacologically increase the peptide concentrations. Finally, radioautographic measurements reveal only modest changes in the concentration of the high affinity SRIF A binding sites, indicating that somatostatin receptor-bearing elements are preserved in the disease. In summary, the somatostatinergic deficit in AD is not a primary event but is likely to intervene in the dementia symptoms. Animal models, such as behaviorally impaired old rats or small primates (*microcebus murinus*) which reproduce partially Alzheimer's disease neuropathology and neurochemical deficits are of interest to assess the potential usefulness of somatostatin derived therapeutical approaches.